LEUCOCYTE PROFILE OF ADULT NIGERIANS AS INDICATOR OF SEVERITY LEVEL IN ACUTE MUSCULOSKELETAL TRAUMA

Abstract:

Leucocytosis, marked increase in the number of white blood cells (WBC) is a known physiological response to trauma. In recent times, several studies have asserted the absence of this response in Africans. In view of this, current study investigated the existence of, and prognostic implications of post-traumatic leucocytosis amongst adult Nigerians with acute musculoskeletal (MSK) trauma. Two hundred and twenty three (223) adult male and females (MSK traumatized) and fifty apparently healthy volunteers (adults) were ethically recruited from the National Orthopaedic Hospital, Enugu, regional centre for trauma, orthopaedic, burns and plastic surgery in south-east Nigeria. Using the Leishman's stained blood smear technique, leucocyte profiles [Neutrophil, Lymphocytes, Basophils, Eosinophils and Monocyte counts] were obtained for each participant. In all case, Age, Gender and duration of hospitalization were also obtained. Following careful analysis, study found, using one way analysis of variance (ANOVA), a statistically significant increase ($p < .05$) in acutely traumatized subjects; with adults of ages 20 to 49 years constituting the majority (70%). A statistically significant lymphopenia was also observed in test population, with Pearson Product Moment Correlation proving positive for higher levels of WBC counts. A negative correlation was also seen for Neutrophils and lymphocyte counts, implicating the Neutrophil-Lymphocyte Stress Factor (NLSF). We recommend the exploration of the NLSF for prognosis of Leucocytosis in Africans.

Keywords: Leucocytosis, Musculoskeletal Trauma, Nigerians

INTRODUCTION

Relative to Caucasians, popular research opinions posit that Africans are leucopenic [1&2]. However, this situation seamlessly affects the occurrence of leukocytosis, which is known to be part of the body's metabolic response to trauma. This response is physiologic, and is geared towards curtailing the effect(s) of trauma of any sort, thereby restoring homeostasis [3].

Trauma is a leading cause of injury and premature death in humans, and its sustained in the body by means of energy exchanges in the course of interaction with the environment. With commonest cause of trauma being road accidents, gunshots and falls from heights, traumatic injuries may include bone fractures, muscular injuries, rupture of tendons and ligaments, etc. With musculoskeletal (MSK) system reportedly composed principally of

about 70% bones, joints, and numerous muscles, the likelihood of its affection due to trauma is significantly huge [4&5].

With recourse to its importance in prognosis of leukocytosis, little or no information exists on the patterns of leucocyte response of Nigerians to acute musculoskeletal injuries. Kho et al., (2003) had suggested that moderate leukocytosis is required for good prognosis following musculoskeletal trauma, whilst linking leukocytosis and leucopenia to increased morbidity and mortality [6]. This suggests that leucocyte profile in acute trauma will be of immense value as MSK trauma becomes a leading cause of mortality and morbidity in developed and developing societies [7].

The consistent increase in circulating free radicals post-trauma has been asserted to be due to the increasing mobilization of circulating polymorphonuclear (PMN) leucocytes in acute traumatization [8]. Muster et al., (2001) while studying activation blood coagulation in pigs after lower limb trauma noticed an increase in serum creatinine kinase, body temperature, metabolic and respiratory alkalosis; as well as in moderate leukocytosis [9]. In literature, the near consistent leukocytosis that follows acute trauma is mostly on studies done on white populations and animal models. Currently, there is dearth of information on black populations living in Africa and their leucocyte response to trauma. Scientifically, prognosticating traumatized Africans with these parameters may be more meaningful if such leukocytosis or other wise is confirmed in our population. Thus, the Acute Physiologic and Chronic Health Evaluation (APACHE) scoring system recognized WBC count as one of the 12 physiological variables measured in acute trauma will be very important for trauma management and prognostication among Africans. Above fact is even more imperative, considering the significant variation in blood parameters of Africans and Caucasians as already established by Ezeilo (2005) [10].

In this study, the total leucocyte count of adult Nigerians who sustained acute musculoskeletal trauma was investigated. The Neutrophil and lymphocyte levels were correspondingly examined and analyzed as well. As control, the WBC profile of apparently healthy individuals were also ascertained to confirm the occurrence(s) of leucopoenia (or otherwise) among adult Nigerians.

Aim of Study

Current study aimed at investigating the occurrence or otherwise, of post-traumatic leucocytosis in adult Nigerians with acute musculoskeletal (traumatic) injuries. Specifically, study attempted to confirm normal leucocyte levels in healthy non-traumatized adult

Nigerians, determine the effect of acute musculoskeletal trauma on leucocyte levels of Nigerians, and to investigate the use of post-traumatic leucocyte level as a prognostic index in traumatology.

Materials and Methods

Study Site

Study was conducted at the National Orthopaedic Hospital, Enugu, a regional centre for trauma, orthopaedic, burns and plastic surgery in south-east Nigeria. The centre is a 250-bed hospital with an accident and emergency unit of 10 beds and 40 couches. The hospital serves 11 states, including those of the south-eastern geopolitical zones plus middle belt states and Abuja, Nigeria's capital

Sample Size

A total of 223 patients were recruited from study site, and decision to sample such (223 subjects) was determined using the relation;

$N = Za^2pq/D3$

Where; N = sample size, Za^2 = standard deviation at 95% = 1.96 distribution, p = 22% prevalence of Musculoskeletal trauma in the area, q = 1 – p and D = standard error = 5% or .05

Procedure

Two hundred and twenty three (233) Nigerian Adults (subjects) of 18 years and above, who had sustained acute musculoskeletal trauma through road traffic accident or elective orthopaedic operations were ethically co-opted into the study. Fifty (50) apparently healthy adult volunteers were also recruited as control. In all case, participants' hospital number, age, sex, and type of injury (acute or chronic) or surgery was recorded. Venous blood was obtained (from the medial cubital vein), and stored in an EDTA bottle for total WBC count using the improved neubauer haemocytometer. Differential counts (Neutrophil, Lymphocyte, Basophil, Eosinophil and Monocyte) were done by microscopic examination of blood films based on the Leishman's stained blood smear method [11]

Inclusion Criteria

Adult males and females (of 18 years and above) with acute musculoskeletal trauma, who had undergone clean elective musculoskeletal surgery, were included. For control, individuals on routine medical check with no trauma, infection or tumour were included.

Exclusion Criteria

Patients with acute or chronic infections that may exacerbate leucocytosis were exempted. Immunocompromised subjects with HIV/AIDS, diabetes, and malignancy were exempted.

Ethical Clearance

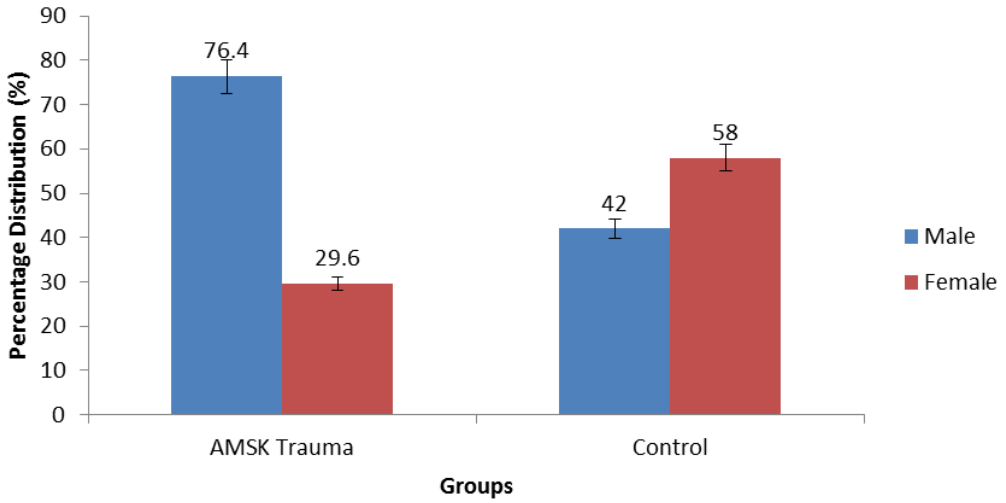
Ethical clearance was obtained from National Orthopaedic Hospital, Ethics Committee, Enugu. Oral and written consents were obtained from participants before commencement of the study.

Statistical Analysis

Data collection was manual, and obtained records were stored in hard and electronic formats. Statistical analysis was done in line with objective of the study, using one way analysis of variance (ANOVA) in any case; results were presented as Mean ± Standard deviation. Differences between mean of test groups were considered significant at $p < .05$.

Results

Figure I: Percentage distribution of subjects by gender



Above figure (Figure I) shows Percentage distribution of subjects by gender where AMSK = Acute Musculoskeletal Traumatized subjects as against the healthy adult control group. As seen, there was a significant distribution ($p < .5$) in incidences of trauma by gender with males dominating (76.4%) for AMSK trauma group than the females. Here, male to female ratio was 4:1 (for test AMSK group), and 3:2 for control group. This sexual variation is suggestive that males sustain more MSK trauma than the females.

Figure II: Percentage distribution of subjects by Age

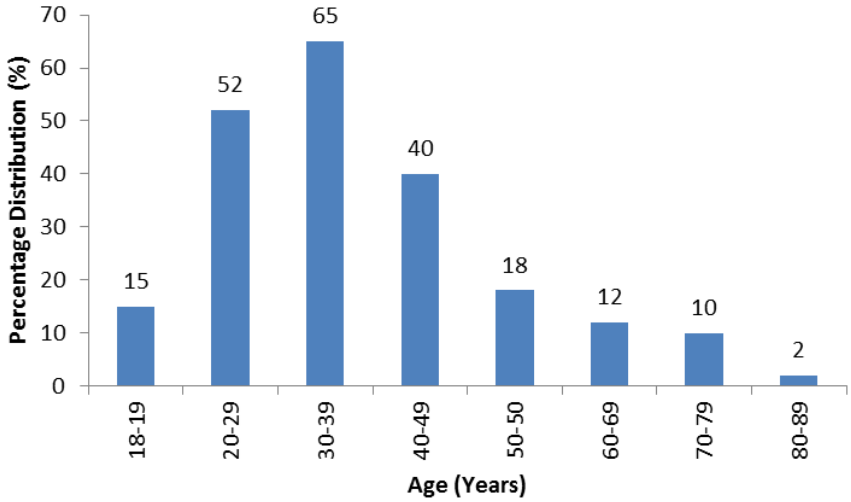


Figure II (above) depicts age distribution of adult Nigerians with acute musculoskeletal trauma. There was a significant variation in the incidence of trauma as age distribution of post-traumatic subjects showed that truama was more prvalent among young productive age group of 20-49 years.

Figure III: Comparison of Average Leucocyte Profile levels of Adult Nigerians

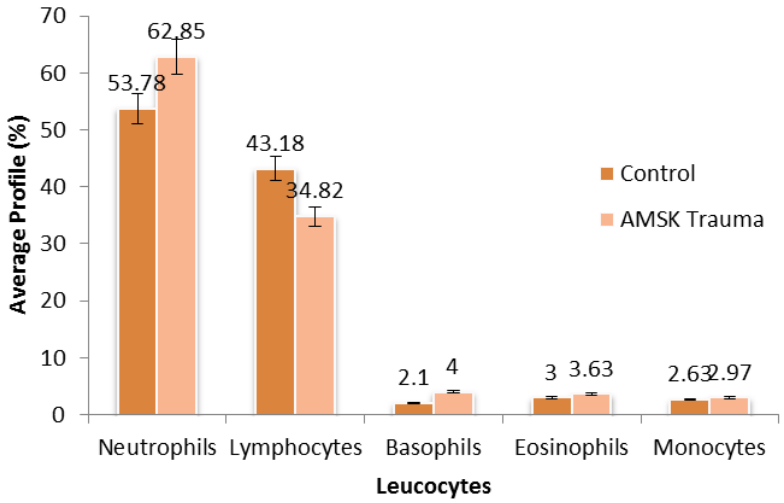
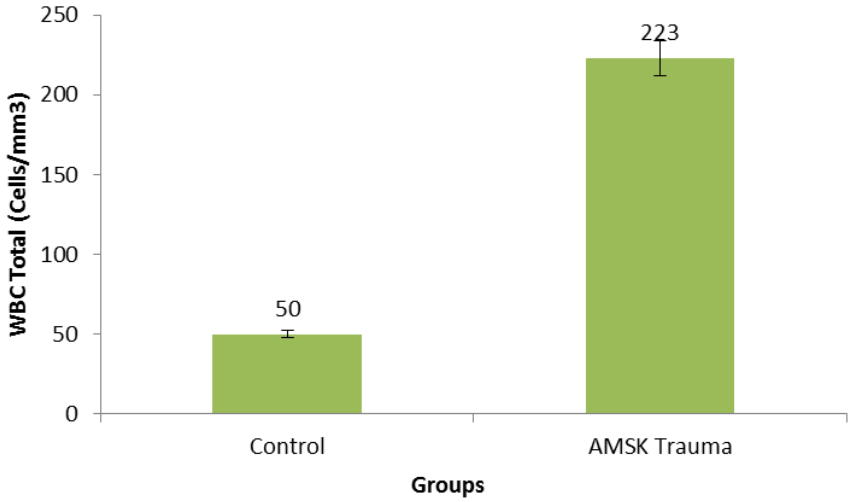


Figure III (above) compares mean leucocyte profile levels of normal (control) and Acute Muscukoskeletal (AMSK) traumatized subjects. Here, average Neutrophil levels was seen to be highest , in AMSK than control subjects with least value observed for basophils in control than AMSK tramatized participants. Also, the comparison of gender to leucocyte profile for control subjects returned a statistically insignificant value with Levene's t-test.

Figure IV: Comparison of Total WBC levels of Adult Nigerians



Above figure (Figure IV) compares total WBC count for healthy (control) and Acute Musculoskeletal (AMSK) Traumatized subjects. Seen here is higher WBCs in AMSK trauma than control group. ANOVA returned a statistically significant increase ($p < .05$) upon comparison.

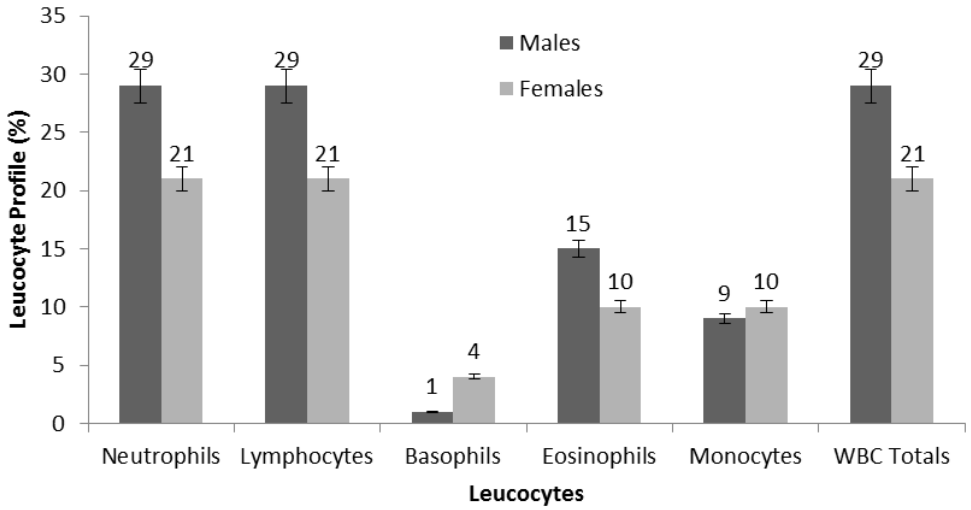
Table I: Descriptive statistics on variations of total WBC count with age in Musculoskeletal Traumatized Subjects

Age Group (Years)	Frequency	Mean	p-value (ANOVA)
18-19	14	7892	.085
20-29	54	8768	
30-39	66	9314	
40-49	41	8500	
50-59	20	9594	

60-69	**14**	**8771**	
70-79	**12**	**8945**	
80+	**1**	**-**	
Total	**223**	**8940**	

Above table presents variations in total WBC counts (by Age) in Musculoskeletal Traumatized Subjects. Here, average WBC count is observed to vary independent of age.

Figure V: Descriptive Gender Comparison of Variations in Leucocyte profiles for Musculoskeletal Traumatised Subjects



From figure V (above), leucocyte profiles of musculoskeletal traumatised subjects shows a statistically significant different difference in leucocyte profile levels across gender comparison with Neutrophils, Lymphocytes and total WBC counts apparently returning same average values across sampled gender.

Discussion

Demographics

Results from this study demonstrate a male preponderance for acute musculoskeletal (AMSK) trauma via traffic accidents or elective orthopaedic surgery as shown in Figure I. The male to female ratio in the study group was seen to be 4:1 which is significant ($p < .05$) as compared to that of the control with a ratio of 3:1. This finding conforms to the report of earlier studies that showed higher incidences of trauma among males than female subjects [12]. This higher incidence in male than female subjects can be attributed to the fact that male sex at all age is more active than their female counterparts [13]. This conforms to a study by Eyichukwu and Iyidobi (2005) that males have greater risky behaviours couple with their

predominant roles as bread winners of the family; causing them to be more exposed to injurious circumstances like road accidents [14].

From this study, trauma was much more prevalent among the young and productive subjects of between 20-49 years which is the age that drives the economy and social activity of any society and accounted for about 72% of sustained musculoskeletal trauma which was significant. Older persons aged 70 years and above are commonly involved in road traffic accidents is another demographic factor that has been documented to affect the incidence of accidental due to their retirement form institutions and incapacitation by one medical condition or the other [15]. This may explain why only 5.8% of the total sampled subjects sustained trauma from 70+ years of age.

Leucocyte Profile

The leucocyte profiles of apparently healthy adult Nigerians (control) confirmed previous reports on the existence of leucopenia in people of African descent compared with those of Caucasoid. Nwobodo et al (2005) while investigating the correlation between Erythrocyte sedimentation rate (ESR) and leucocyte counts in Nigerians noted a general leucopenia amongst his subjects; though those who had evidence of chronic leuco-neutropenia in a Nigerian population was evaluated. Their report showed a clear leuco-neutropenia amongst Nigerian adults [2]. A recent work by Anyaehie et al (2007) also agrees with the result of this work [16]. They had investigated the leucocyte profile of apparently healthy prospective blood donors in Owerri and observed a consistent result with African leucopenia, which has been widely cited [10]. The inconsistent report about the true cause of African leucopenia is yet to be resolved. Such reports vary from chronic infection and dietary cause to genetic factors as possible etiological factors.

For current study, leucocyte profile of traumatized group showed demonstrable post-traumatic leukocytosis with mean total WBC count found to be 8184 cells/mm^3 (table I). This is significantly higher than the mean for control group (4922 cells/mm^3) at $p < .05$. this finding clearly contrasts the report of Change (2003) who analysed post-traumatic leucocyte count among different races and postulated that only white race and severity of trauma were associated with acute increase in total WBC count[3]. This conclusion that black people do not exhibit post-traumatic leukocytosis could no longer subsist, given the result of current study. Thus, acute infection [17] and exercise [18] also induce acute leukocytosis in Nigerians and possibly others of African origin. This finding collaborates the result of a study in lagos

in which leucocyte response to surgical trauma in Nigerians was investigated. The authors showed that the peripheral blood leucocyte count and neutrophils were significantly increased by one hour after major surgery, and that this increase was sustained for a minimum of 7 days after trauma [19]. Their conclusion was that the leucocyte and polymorphonuclear neutrophils response to acute surgical trauma in Nigerians was similar to previous observations made in Caucasians.

The exclusion of subjects with open wounds, burns, etc from the test group allows the conclusion that trauma was the underlying factor responsible for the observed leukocytosis. Early leukocytosis following trauma has been previously attributed to the presence of bacteria in blood and infection led to the delays in the institution of appropriate treatment modalities. It has been suggested that bacteria is not the leading cause of fever and leukocytosis in those who sustain acute and severe traumatic injuries [19]. This implicates trauma as the likely cause of post-traumatic leukocytosis. Similarly, Golob et al (2008) had shown that urinary tract infection was not the cause of majority of the observed fever and leukocytosis in the acutely traumatized [20]. They therefore concluding that emphasis needs not placed on infection as the source of fever and leukocytosis in injured subjects during the first 14 days following injury since trauma also leads to inflammation and fever.

Physiologic and Clinical Implications

Findings from current study will be of immense physiological importance as it clearly shows the relationship between trauma, inflammation, fever and leucocytosis. Thus, early damage control surgeries like debridement and fracture stabilization can be carried out as emergency [21] with a view to reducing the morbidity of unabated metabolic response to trauma and thereby improve outcome. This is even more compelling as researchers continue to point at WBC levels as a possible indicator of severity of trauma as well as predictor of outcome. Rovalias (2008) showed that patients with severe head injury had significantly higher WBC counts than those with moderate or minor injury [22]. He found a significant relationship between WBC counts and papillary reaction. Very high WBC counts were also found in those that had unfavorable outcomes. He thus concluded that WBC count was an independent predictor of outcomes in severe trauma. This view is strongly supported by the correlation test from this study. Duration of hospitalization, a known prognostic index was found to correlate positively with higher value of total WBC count ($p < .05$). Patients with higher WBC counts were hospitalized for longer periods possibly because they had more severe

injuries. Such patients with very high WBC counts could be isolated early for more aggressive modes of treatments and observation including intensive care unit (ICU) admission with early operative fixation of fractures to improve outcome and thus shorten duration of hospitalization.

There are several advantages of using WBC count as index of severity of injury in blunt trauma patients. The traditional parameters include injury security score (ISS), Glasgow Coma Scale (GCS) and Revised Trauma Score (RTS). ISS is too complicated, while GCS and RTS are subjective and observer dependent. WBC on the other hand is easy, quick, observative and readily available, and thus can be applied at least as a useful adjunct in the evaluation of severity of trauma [4].

There is rich evidence in the literature that trauma induced leucocytosis is mainly due to neutrophilia caused by demargination of neutrophils [23] as well as stimulation of bone marrow by cytokines elaborated acutely in trauma. This is supported by the finding of a significant neutrophilia among the test population in this study (Figure V). Bastian et al (2009) clearly showed a significant acute post-traumatic rise in monocyte and neutrophil levels as well as total WBC count amongst subjects who had total hip replacement arthroplasty [24]. This work confirmed that chemokine burst arising from tissue damage was responsible for the observed neutrophilia and monocytaemia. This also supports the report of Olav (2010) who noted that monocytes and macrophages are responsible for the inflammatory response syndrome and subsequent organ dysfunction seen in severe trauma. Thus, a high absolute neutrophil count in severe trauma is associated with increased morbidity and mortality [21].

Lymphopenia and Neutrophil Lymphocyte Stress Factor

From current study, there was post-traumatic lymphopenia among test subjects (34.82 ± 11.38%). Lymphopenia is a documented parameter following acute traumatic injury. It is seen in inverse relationship with neutrophil and has been advocated as an index of severity of trauma [12]. This inverse relationship is clearly shown by the strong negative correlation between the levels of lymphocyte and neutrophils among the test population. Zahorec in 2001 investigated the ration of neutrophil to lymphocyte count in subjects that underwent major surgical operations and noted that the ratio in absolute and/or relative values was an easily measurable parameter that may express the severity of surgical and hence, traumatic stress. This is because of the consistency in their divergent and inverse values [25]. They therefore

suggested that the term Neutrophil Lymphocyte Stress Factor (NLSF) as a ratio of neutrophil to lymphocyte counts can be of clinical use in post-traumatic and other patients admitted to intense care units. This suggestion is gaining ground. Similarly, there is evidence of lymphopenia and abnormal T-lymphocyte function following orthopedic trauma. There is also evidence that the near consistent poor outcome of trauma associated with extreme lymphopenia is due to apoptosis and development of severe T-cell depletion resulting in energy and subsequent organ failure [26]. The effect of age and sex on the leucocyte profile of the post traumatic subjects was found to be insignificant. This is contrary to documented evidence of metabolic response to trauma being more pronounced in young male adults. Waters et al (2000) however studied the effect of age and body composition on metabolic response to elective surgical trauma and found that serum glucose, cortisol, WBC count and c-reactive proteins were independent of age [27]. This was corroborated by the result of this study.

Conclusion

Current study has shown that adult Nigerians who exhibit post-traumatic leukocytosis and ethnic leucopenia had no effect on the expected leucocytosis. This is in contrast with suggestions that Africans do not exhibit post-traumatic leucocytosis in some western publications. This study also saw a strong positive correlation between the higher levels of leucocytosis and prolonged hospitalization in weeks. Hence, patients who had higher total WBC count stayed longer in hospital and were more likely to have sustained more trauma than others. These groups of patients would have benefited from more aggressive treatment modalities.

Recommendations

In management of post-traumatic Nigerian patients, we recommend that leucocyte values should be an index of trauma severity in clinical practice. We also recommend the application of Neutrophil Lymphocyte Stress Factor in assessment and prognosis of post-traumatic subjects. A multi-centre double blinded study that involves much number of subjects is recommended for possible clinical application of this study.

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